

## CLAIMS

### WHAT IS CLAIMED IS:

1. A method of eliciting broad spectrum protective immunity against *Neisseria meningitidis*, said method comprising the steps of:  
administering to a mammal a first preparation of microvesicles (MVs) from a first *Neisseria meningitidis* species that is a member of a first serotype and of a first serosubtype, in an amount sufficient to elicit an immune response to epitopes present in said first preparation;  
and  
administering to said mammal a second preparation of MVs from a second *Neisseria meningitidis* species that is a member of a second serotype and of a second serosubtype, in an amount sufficient to elicit an immune response to epitopes present in said second preparation;  
wherein the serotype or serosubtype of each of the first, second, and third *Neisseria meningitidis* species is different, and wherein administering of the first, second, and third preparations is sufficient to elicit an immune response in said mammal, wherein said immune response confers protective immunity against a disease caused by more than one strain of *Neisseria meningitidis* species.
2. The method of claim 1, the method further comprising:  
administering to said mammal a third preparation of outer membrane vesicles (OMV), MVs, or both OMVs and MVs from a third *Neisseria meningitidis* species that is a member of a third serotype and of a third serosubtype, in an amount sufficient to elicit an immune response to epitopes present in said third preparation.
3. The method of claim 2, wherein the first, second, and third preparations are administered serially.

4. The method of claim 3, wherein the preparations are administered such that the first preparation is administered first, the second preparation administered second, and third preparation administered third.

5. The method of claim 1, wherein the first, second, and third preparations are administered as a mixture.

6. The method of claim 1, wherein the third preparation comprises MVs.

7. The method of claim 1, wherein the protective immunity conferred is against a disease at least four strains of *Neisseria meningitidis* species.

8. The method of claim 7, wherein protective immunity conferred is against a disease caused by more than one strain of serogroup B *Neisseria meningitidis* species.

9. A method of eliciting broad spectrum protective immunity against a disease caused by a member of serogroup B of *Neisseria meningitidis*, said method comprising the steps of:  
administering to a mammal a first preparation of microvesicles (MVs) from a first *Neisseria meningitidis* species that is a member of a first serosubtype, in a amount sufficient to elicit an immune response to epitopes present in said first preparation;

administering to said mammal a second preparation of MVs from a second *Neisseria meningitidis* species that is a member of a second serosubtype, in a amount sufficient to elicit an immune response to epitopes present in said second preparation;

wherein the serosubtype of each of the first and second *Neisseria meningitidis* species is different, and wherein administering of the first and second preparations is sufficient to elicit an immune response in said mammal, wherein said immune response confers protective immunity against a disease caused by at least four strains of *Neisseria meningitidis* species.

10. The method of claim 9, wherein the method further comprises administering to said mammal a third preparation from a third *Neisseria meningitidis* species that is a member of a third serosubtype, the third preparation comprising outer membrane vesicles (OMV), MVs, or both OMVs and MVs, said administering being in an amount sufficient to elicit an immune response to epitopes present in said third preparation, wherein the serosubtype of the first and third species is different.

11. The method of claim 10, wherein the serosubtype of the first, second, and third species is different.

12. The method of claim 9, wherein the first and second preparations are administered as a mixture.

13. The method of claim 9, wherein the first and second preparations are administered serially.

14. A method of eliciting broad spectrum protective immunity against a disease caused by a *Neisseria meningitidis* species, said method comprising the steps of:

administering to a mammal a first preparation from a first *Neisseria meningitidis* species, the first preparation comprising outer membrane vesicles (OMV), microvesicles (MV), or both OMV and MV, said administering of the first preparation being in an amount sufficient to elicit an immune response to epitopes present in said first preparation;

administering to the mammal a second preparation from a second *Neisseria meningitidis* species that is genetically diverse to the first *Neisseria meningitidis* species, the second preparation comprising outer membrane vesicles (OMV), microvesicles (MV), or both OMV and MV, said administering of the second preparation being in an amount sufficient to elicit an immune response to epitopes present in said second preparation;

wherein administering of the first and second preparations elicits an immune response in said mammal, wherein said immune response confers protective immunity against a disease caused more than one strain of *Neisseria meningitidis* species.

15. The method of claim 14, comprising the additional step of administering to said mammal a third preparation of outer membrane vesicles from a third *Neisseria meningitidis* species, which third species that is genetically diverse to at least the first *Neisseria meningitidis* species, said administering being in an amount sufficient amount to elicit an immune response to epitopes present in said third preparation.

16. A method for eliciting broad spectrum protective immunity against a disease caused by a *Neisseria meningitidis* species, said method comprising the steps of:

administering to a mammal a first antigen preparation from a first *Neisseria meningitidis* species, said administering of the first preparation being in an amount sufficient to elicit an immune response to epitopes present in said first preparation;

administering to the mammal a second antigen preparation from a second *Neisseria meningitidis* species that is genetically diverse to the first *Neisseria meningitidis* species, said administering of the second preparation being in an amount sufficient to elicit an immune response to epitopes present in said second preparation;

wherein administering of the first and second preparations elicits an immune response in said mammal, wherein said immune response confers protective immunity against a disease caused more than one strain of *Neisseria meningitidis* species.

17. The method of claim 16, wherein the method further comprises administering to the mammal a third antigen preparation from a third *Neisseria meningitidis* species that is genetically diverse to at least the first *Neisseria meningitidis* species, said administering of the third preparation being in an amount sufficient to elicit an immune response to epitopes present in said second preparation;

18. The method of claim 16 wherein the first and second antigen preparations are administered serially.

19. The method of claim 16 wherein the first and second antigen preparations are administered as a mixture.

20. The methods of claims 1, 9, 14 or 16 wherein the OMV and MV preparations are administered together with pharmaceutically acceptable excipients.

21. The method of claims 1, 9, 14 or 16, wherein the excipients comprise an adjuvant.

22. The method of claims 1, 9, 14 or 16, wherein the adjuvant is selected from the group consisting of aluminum phosphate, aluminum hydroxide, alum or MF59.

23. The method of claims 1, 9, 14 or 16, wherein administering is by injection.

24. The method of claims 1, 9, 14 or 16 wherein administering is oral or by aerosol administration.

25. The method of claims 1, 9, 14 or 16, wherein the mammal is a human.

26. The method of claim 25, wherein the human is immunologically naïve with respect to *Neisseria meningitidis*.

27. The method of claim 25, wherein the human is a human child less than five years old.

28. A method of identifying an antigenic epitope that elicits broad spectrum protective immunity against a disease caused by *Neisseria meningitidis* species, said method comprising the steps of:

administering to a mammal a first preparation of outer membrane vesicles (OMV), microvesicles (MV), or both OMV and MV from a first *Neisseria meningitidis* species, said administering being in an amount sufficient to elicit an immune response to epitopes present in said first preparation;

administering to said mammal at least a second preparation of outer membrane vesicles (OMV), microvesicles (MV), or both OMV and MV of a second *Neisseria meningitidis* species, in an amount sufficient to elicit an immune response to epitopes present in said second preparation, wherein the second *Neisseria meningitidis* spp is genetically diverse to the first *Neisseria meningitidis* spp, and wherein said administering of the first and second preparations is sufficient to elicit an immune response to at least one epitope present in said first and second preparations, and wherein said response confers protective immunity against a disease caused by *Neisseria meningitidis* species; and

identifying at least one epitope that elicits broad spectrum protective immunity against a disease caused by *Neisseria meningitidis* species.

29. A composition comprising:

a first preparation selected from the group consisting of outer membrane vesicle (OMV), microvesicles (MV), or both OMV and MV from a first from a first *Neisseria meningitidis* species; and

a second preparation selected from the group consisting of outer membrane vesicle (OMV), microvesicles (MV), or both OMV and MV from a second *Neisseria meningitidis* species, wherein the second *Neisseria meningitidis* spp is genetically diverse to the first *Neisseria meningitidis* species; and

a pharmaceutically acceptable carrier.

30. The composition of claim 29, further comprising:

a third preparation selected from the group consisting of outer membrane vesicle (OMV), microvesicles (MV), or both OMV and MV from a third *Neisseria meningitidis* species, wherein the third *Neisseria meningitidis* species is genetically diverse to the first *Neisseria meningitidis* species.

31. The composition of claim 30, wherein:

the first preparation comprises MV;

the second preparation comprises MV; and

the third preparation comprises OMV.

32. The composition of claim 29, wherein the first and second *Neisseria meningitidis* species are genetically diverse in that they differ in at least one of serotype, or serosubtype.

33. The composition of claim 31, wherein the first and third *Neisseria meningitidis* species are genetically diverse in that they differ in at least one of serotype, or serosubtype.

34. A composition comprising:

at least one isolated *Neisseria meningitidis* antigen, the isolated antigen being present in the composition in an amount effective to elicit an immune response in a mammalian host, and being characterized as a protein immunoprecipitated with anti-sera produced following vaccination of a mammal with the composition of claim 31, and having an apparent molecular mass selected from the group consisting of about 80 kDa, about 59.5 kDa, about 40.7 kDa, about 39.6 kDa, about 33 kDa, about 27.9 kDa, and 14.5 kDa; and

a pharmaceutically acceptable excipient.

35. A composition comprising:

at least one isolated *Neisseria meningitidis* antigen, the isolated antigen being present in the composition in an amount effective to elicit an immune response in a mammalian host,

and being characterized as a protein detected by Western blot with anti-sera produced following vaccination of a mammal with the composition of claim 31, and having an apparent molecular mass selected from the group consisting of about 53 kDa to 57 kDa; about 46-47 kDa, about 33 kDa, about 20 kDa to 21 kDa; and about 18 kDa; and  
a pharmaceutically acceptable excipient.

36. A composition comprising:

at least one isolated *Neisseria meningitidis* antigen, the isolated antigen being present in the composition in an amount effective to elicit an immune response in a mammalian host, wherein the antigen is from a protein that specifically binds a monoclonal antibody selected from the group consisting of 1D9 (ATCC Accession No. xx), 4B11 (ATCC Accession No. xx), 9B8 (ATCC Accession No. xx), and 14C7 (ATCC Accession No. xx); and  
a pharmaceutically acceptable excipient.

37. The composition of claim 34, 35, or 36, wherein the composition comprises at least two isolated *Neisseria meningitidis* antigens.

38. A composition comprising isolated *Neisseria meningitidis* antigens, wherein said antigens are identified by the method of claim 28.

39. A method for eliciting broad spectrum protective immunity against a disease caused by a *Neisseria meningitidis* species, said method comprising administering to a mammal the composition of claim 34, 35, 36, or 38.